Is there a role for parenteral nutrition or hydration at the end of life?

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Purpose of review
This review aims to update healthcare providers on the role of parenteral nutrition/hydration in terminal patients and highlight recent research.

Recent findings
Cachexia is felt to be refractory to treatment at the last stages of life. The majority of terminally ill patients will derive no benefit from parenteral nutrition with some exceptions including patients with a good functional status and a nonfunctional gastrointestinal tract or a slow growing tumor.
Dehydration can potentially be reversible in patients at the end of life. However, recent research examining parenteral hydration reveals no clear clinical benefits on symptom burden or survival for terminally ill cancer patients with the exception of possibly reversing the complication of delirium.

Summary
Hydration and nutrition are essential for the maintenance of life. In patients at the end of life, artificial hydration and nutrition pose clinical, ethical, and logistical dilemmas. No strong evidence exists supporting the use of parenteral hydration/nutrition for the majority of terminally ill patients; however, a subset of patients may derive some benefit. Uncertainty about determining prognosis, psychosocial factors, and perceptions of perceived benefits results in artificial nutrition/hydration being initiated in terminally ill patients. Discontinuation of artificial support can result in distress for patients, family members, and healthcare providers.

Keywords
artificial hydration, artificial nutrition, palliative care, parenteral nutrition, terminal illness

INTRODUCTION

Hydration and nutrition are essential for the maintenance of life. In patients at the end of life (survival days or weeks), artificial hydration and nutrition pose clinical, ethical, and logistical dilemmas resulting in debates for and against such interventions. No strong evidence exists supporting the use of parenteral hydration and nutrition for terminally ill patients; however, a paucity of research examining the issue exists. This review aims to update healthcare providers on the role of artificial nutrition/hydration in terminally ill patients and highlight recent research.

Currently, there are differences in perceived benefits of artificial nutrition/hydration between healthcare providers and the general public [1▪]. Wide variations in practice patterns exist depending on the setting (inpatient versus hospice) [2]; culture (Dutch doctors often take primary responsibility for providing artificial nutrition and hydration versus Australian physicians who are more likely to let the patient's family make the decision) [3▪]; and field of expertise (Japanese oncologists were noted to perceive more benefit versus their palliative care colleagues) [4]. As a possible result of these variations, communication provided by healthcare providers about artificial nutrition/hydration is inconsistent which results in confusion for patients and family members. In addition, patients and family members are often not involved in the decision-making [5]; and when they do participate, their decisions are

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KEY POINTS

- The majority of terminally ill patients will derive no benefit from parenteral nutrition, with some exceptions that include patients with a good functional status and a nonfunctional gastrointestinal tract or a slow growing tumor.
- No clear benefits of parenteral hydration on symptom burden or survival for terminally ill cancer patients.
- Discontinuation of artificial nutrition or hydration can result in distress for patients, family members, and healthcare providers.

influenced by their physicians' recommendations [6].

Adding to the confusion is the emotional nature of these discussions. When patients with a life-limiting illness are unable to adequately take in nutrition and fluids, the issue of starvation and eventual death rises to the forefront [7]. In the clinical setting, it is not uncommon for distressed patients, who are unable to eat or drink, and their family emotionally pleading with healthcare providers to intervene. Once parenteral nutrition or hydration is initiated, it often takes clear and consistent dialog between family and empathetic healthcare providers to convince patients to discontinue these artificial measures. A recent survey of 663 physicians practicing palliative care providers reported that the act of stopping artificial hydration/nutrition, along with palliative sedation, was misconstrued as euthanasia [8▪]. In the same study, 32% of the cases of allegations of euthanasia were initiated by the healthcare team highlighting that even healthcare professionals have difficulty with these clinical scenarios and disagree with what is best for the patient.

In addition to the emotionally charged nature of discussions regarding the discontinuation of parenteral nutrition/hydration, there are uncertainties about when to withdraw artificial nutritional support. Predicting prognosis is difficult, and existing terminology including 'terminal illness' and 'end of life' are ambiguous [9–11], which makes the decision at what point in the illness trajectory to forgo or discontinue artificial hydration and nutrition for terminally ill patients even more difficult.

NUTRITION

Patients during the last days and weeks of life often have anorexia – decreased oral intake – resulting in cachexia, which is loss of body weight with reduced muscle mass and adipose tissue. In addition, cancer patients, frequently gastrointestinal or gynecologic malignancies, may develop mechanical obstruction of the digestive tract preventing enteral nutrition [12]. In the last stages of life, cachexia was considered by an international consensus of experts to be refractory to treatment [13▪]. In these patients, the goals of therapy should be directed at symptoms rather than reversing nutritional deficits. The pleasure of tasting food and the social benefits of participating in meals with family and friends should be emphasized over increasing caloric intake.

In terminally ill patients with cachexia, tube feeding or parenteral nutrition is often requested by patients and their family. In a study assessing the quality of end-of-life care, artificial nutrition was often initiated without documentation of discussions regarding prognosis and the terminal nature of an illness [14▪]. Another 1-day observational study in Belgium reported artificial nutrition was being considered, planned, or ongoing in 50% of hospitalized patients at the end of life with the goal of controlling symptoms in 66% of the cases, as opposed to prolongation of life [15]. A systematic review examining the frequency of artificial nutrition, both tube feeding and total parenteral nutrition, reported a range between 35 and 50% with a higher utilization on nonpalliative hospital wards (range 8–53%) compared with palliative wards (range 3–10%) [1▪]. The authors suggest that the diagnosis of dying occurs more frequently in a palliative or hospice setting resulting in less use of artificial nutritional support. Healthcare professionals often provide artificial nutrition to accommodate patient and family members requesting such interventions while often avoiding discussions about the terminal nature of a patient's illness. Arguably, palliative care and hospice providers communicate prognosis more effectively and may facilitate greater acceptance of death in both patients and their family, minimizing the use of artificial nutrition.

Patients and their family often perceive benefits for artificial nutritional support at the end of life. A qualitative study of 13 advanced cancer patients and 11 family members reported that home parenteral nutrition provided psychological benefits associated with a sense of relief that the patients nutritional requirements were met which prevailed over the burden of restriction of movement and limitation of contact with family and friends [16]. In Sweden, a recent telephone survey of patients enrolled in palliative care services noted that home artificial nutrition – parenteral nutrition was more common (11%) than enteral tube feeding (3%) – was introduced more than 4 months before death and mainly used to treat eating difficulties, symptoms of

nausea/vomiting, and fatigue rather than a nonfunctional gastrointestinal tract [17]. In the same study, researchers reported that parenteral nutrition had no affect on appetite in the majority of patients, increased appetite in roughly 25%, and decreased in 16% patients.

The majority of patients in the last days or weeks of life will unlikely benefit from parenteral nutrition. A Cochrane review of artificial nutrition in adult patients during the dying phase examining randomized controlled trials and high-quality prospective studies concluded insufficient evidence to make recommendations [18]. Another review examining a 100 randomized controlled trials in patients who were not necessarily classified as terminally ill, found no evidence to support parenteral nutrition with the exception and uncertainty in a few scenarios; parenteral nutrition initiated in the preoperative setting in patients undergoing curative surgery was noted to reduce postoperative complications; conflicting evidence of benefit of parenteral nutrition in patients undergoing bone marrow transplantation; and evidence of harm in cancer patients undergoing chemotherapy or radiation treatment [19].

In some clinical scenarios, when a functional patient has a slow-growing malignancy and symptoms of starvation, parenteral nutrition may be considered. The European Association for Palliative Care recommends consideration for parenteral nutrition in patients with a good performance status and life expectancy of greater than 3 months who may die of anorexia/cachexia rather than their malignancy [20]. Prior to initiation of parenteral nutrition, patients and family members should be aware of potential complications including catheter infections, thrombosis, pneumothorax, fluid overload, and liver disease [21].

In 115 adult patients with malignant gastrointestinal obstruction, a retrospective study reported a median time from initiation of parenteral nutrition to death of 6.5 months with 11 patients surviving greater than a year and 2 patents who were alive for up to 4 years [22]. A recent prospective study revealed that cancer patients with gastrointestinal obstruction on parenteral nutrition had a longer survival, which correlated with a higher performance status, but an increased rate of infectious complications per treatment days when compared to nonmalignant gastrointestinal failure [23▪].

More research is required to delineate the subgroup of patients at the end of life who may benefit from parenteral nutrition, and also to examine the psychosocial factors which lead patients, family members, and healthcare providers to initiate artificial nutritional support at the end of life.

HYDRATION

Majority of patients at the end of life reduce their oral intake of fluids due to many causes such as anorexia, nausea and vomiting, dysphagia, bowel obstruction, cognitive impairment, or general frailty. Dehydration in turn can cause or aggravate pre-existing symptoms such as fatigue, sedation, and delirium. Proponents argue that hydration is a basic human need and can reduce and prevent dehydration-induced delirium, opioid neurotoxicity, and/or fatigue in terminally ill patients. Others have argued that parenteral hydration is burdensome and prolongs the dying process. Nurses delivering hospice care report that patients under their care frequently achieve a 'good death' without receiving food or hydration [24]. The arguments for and against parenteral hydration at the end of life are summarized in Table 1 [25]. There is scarcity of scientific evidence to support either approach, with only a handful of prospective or randomized controlled trials that have been conducted in patients at the end of life. Formal clinical trials to address the potential symptomatic and survival benefits of artificial hydration are difficult to conduct because of methodological and ethical reasons.

With no established standards for hydration at the end of life, the decision to implement artificial hydration presents challenges for healthcare providers. Two key questions in the hydration debate are whether dehydration causes distressful symptoms in patients who are terminally ill, and if administration of parenteral hydration in those with absent or restricted oral intake is beneficial in improving symptoms or quality of life (QoL).

There are conflicting reports with regards to the association between symptoms and presence of dehydration at the end of life. Whereas many studies have reported high symptom burden in association with decreased oral intake [26], others have observed symptoms to be present irrespective of hydration status [27]. For instance, the symptom of thirst is often a concern for patients and their family, when there is reduced oral intake. However, studies suggest only a modest correlation between the sensation of thirst and hydration status in terminally ill patients [27,28]. Often, thirst can be symptomatically managed with small amounts of oral fluids and good oral hygiene [29]. A small randomized controlled trial (conducted in the last 4 days of life) found no benefit of parenteral hydration over mouth care [30].

Another plausible rationale for administrating fluids is to prevent or treat agitated delirium, which is a frequent and devastating symptom for dying patients, their families, and healthcare professionals [31–33]. Opioid-induced neurotoxicity (OIN)

Table 1. Hydration debate

Arguments for hydration	Arguments against hydration
Provides a basic human need	Interferes with acceptance of the terminal condition
Provides comfort and prevents uncomfortable symptoms: confusion, agitation, and neuromuscular irritability	Intravenous therapy is painful and intrusive
Prevents complications (e.g. neurotoxicity with high-dose narcotics)	Prolongs suffering and the dying process
Relieves thirst, recognized as a sign of fluid needs	Unnecessary as unconscious patients do not experience
Does not prolong life to any meaningful degree	Uncomfortable symptoms, such as pain or thirst
Allows providers to continue their efforts to find ways to improve comfort and life quality, despite the perception of a poor quality of life	Less urine output means less need for bed pan, urinal, commode, or catheter
Provides minimum standards of care; not doing so would break a bond with the patient	Less fluid in the gastrointestinal tract and less vomiting
May set a precedent to withhold therapies from other patients who are compromised	Less pulmonary secretions and less cough, choking, and congestion
	Minimizes edema and ascites
	Ketones and other metabolic byproducts in dehydration act as natural anesthetics for the central nervous system, causing decreased levels of consciousness and decreased suffering

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manifests with varying degrees of sedation, cognitive impairment, hallucinations, myoclonus, or hyperalgesia and are due to accumulation of toxic opioid metabolites [34]. Hydration may prevent the accumulation of opioid metabolites as well as other drugs and plausibly result in the improvement or prevention of delirium [35,36]. Observational and retrospective studies conducted in advanced cancer and elderly patients suggest that hydration intervention may help in delirium prevention [37], or its reversal with improved symptoms in majority of patients [38]. In patients with OIN, a study suggested the presence of fluid deficits to be associated with delirium reversibility [39], and hydration therapy (along with opioid adjustment/rotation) was beneficial in one study [40] but not so in another [41].

In 2008, a Cochrane review of hydration for patients receiving palliative care concluded a lack of high-quality evidence to recommend hydration [42]. An initial randomized controlled, double-blind pilot study was completed examining parenteral hydration (1000 ml normal saline per day) with placebo (100 ml/day) for 2 days, in 49 terminally ill cancer patients receiving home hospice care with mild to moderate dehydration and an oral intake less than 1000 ml daily [43]. At the end of study, patients were evaluated for target symptoms (hallucinations, myoclonus, fatigue, and sedation), global well being, and overall benefit. The hydration group demonstrated significant improvements in sedation and myoclonus as compared with the placebo group, whereas there was no difference for symptoms of fatigue, hallucinations, well being, or perceived overall benefit.

A recently completed, large, randomized controlled, double-blinded study was conducted by the same group in a similar population of terminally ill cancer patients in the home hospice care setting with longer intervention period [44]. This study evaluated the benefits of hydration on days 4 and 7, on symptom burden, delirium onset, QoL, and survival. The median survival of study participants was 17 days. This study did not find hydration (at 1000 ml/day) to be superior to placebo (100 ml/day) in improving on the following target symptoms: hallucinations, myoclonus, fatigue and sedation, QoL, or survival (manuscript submitted) [44]. These findings suggest that there may be no clinical benefits for hydration on symptoms burden or survival in terminally ill patients with a prognosis of days to weeks, and support other preliminary studies [30,41,45]. Of note, patients with severe signs of dehydration, or with delirium, were excluded from participation in the study which did reveal a trend for decreased frequency of delirium at day 4 following intervention in the hydration group. Further studies are needed to determine if parenteral hydration may benefit a subgroup of patients such as those with delirium or a better prognosis.

Despite the lack of clinical benefits, qualitative studies reported that advanced cancer patients and families viewed parenteral hydration as enhancing comfort, dignity, and QoL [46▪]. Discussions with

patients and their family regarding their preferences may result in a decision to rehydrate. If treatment is desired, subcutaneous hydration (hypodermoclysis) is a useful and comfortable alternative to intravenous hydration [47]. This simple and well tolerated technique can be easily applied in the home setting and can minimize the cost of providing hydration for patients at the end of life.

CONCLUSION

When patients approach the end of life, they often have severely restricted oral intake of food and fluids. The decision to administer parenteral nutrition and/or fluids should be individualized, based upon the clinical scenario, and be consistent with the goals of care of the patient. In case of uncertainty of the benefits and risks of parenteral nutrition/hydration in a particular patient, a brief trial with clearly defined goals would be appropriate to initiate, followed by re-assessments of its clinical benefits and harm. Arguably, the decision to offer parenteral hydration/nutrition or not revolves less around the benefits versus risks of the intervention, but whether or not terminally ill patients and their family have emotionally accepted the fact the patient is dying. Further studies are needed to determine which subgroup of patients at the end of life will respond to parenteral nutrition/hydration and also examine the complex psychosocial requirements of terminally ill patients and their family for oral intake of food and water and ways for healthcare providers to compassionately intervene in order to lessen their distress.

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Conflicts of interest

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